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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,055	06/20/2003	Uwe Ries	1/1358	5854
28501	7590	07/03/2007		
MICHAEL P. MORRIS BOEHRINGER INGELHEIM CORPORATION 900 RIDGEBURY ROAD P. O. BOX 368 RIDGEFIELD, CT 06877-0368			EXAMINER WANG, SHENGJUN	
			ART UNIT 1617	PAPER NUMBER
			MAIL DATE 07/03/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,055	RIES ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-11 and 13-19 is/are pending in the application.
- 4a) Of the above claim(s) 7-10 and 13-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-6,11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted April 3, 2007 is acknowledged.

Claim rejections 35 U.S.C. 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
3. Claim 3 depends on claim 2, which was cancelled. The claim is indefinite as to the method steps encompassed thereby. For compact prosecution, claim 3 is treated as depending on claim 1 in following art rejection.

Claim Rejections 35 U.S.C. 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1, 3-6, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ries et al. (WO00/01704, or 6,248,770 as English equivalent, IDS), in view of Romisch et al.

Art Unit: 1617

(EP 1 027 894), Tsukada et al. (EP 0 781 558) and Iqbal et al. and in further view of Merck Manual regarding bacteraemia.

6. Ries et al. teaches that the compounds herein, including their stereoisomers, are known as antithrombotic pharmaceutical agents. The elected compound 2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(carboxymethylamino)-1-(pyrrolidin-1-yl-carbonyl)-ethyl]-benzimidazole is one of the preferred compounds. See, particularly, the abstract, the examples, and the claims. As racemics, the compounds may be separated into enantiomers by conventional method. The compounds may be used in the forms of any pharmaceutical acceptable salts, including salt with hydrochloric acid. See col. 19, line 45 to col. 20, line 15 in '770.

7. Ries et al. do not teach expressly the employment of the particular antithrombotic agent for treating sepsis, or related disorders, bacteraemia.

However, Romisch et al. Tsukada et al. and Iqbal et al. disclosed that antithrombotic agents (such as antithrombins) have been known as useful for treatment of sepsis. See, particularly, the abstracts and the claims of both Tsukada et al. and Romisch et al. and the abstract of Iqbal et al. Sepsis, is an stage of Systemic inflammatory responsive syndrome, and often arise from bacteraemia (Merck Manual). Microvascular thrombosis and disseminated intravascular coagulation are the common symptoms for sepsis. See, columns 1-2 in Romisch et al. and pages 111-115 of Iqbal et al. It is also known in the art that anticoagulants agent, including those of antithrombotic agents are expected to be useful for treating sepsis. See, page 118 and 119 in Iqbal et al.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ the compound herein for the treatment

Art Unit: 1617

or prophylactic treatment of sepsis, including for those patients suffering from bacteraemia. The employment of the particular compound as the antithrombotic agent is obvious as it is disclosed as one of the preferred compounds. The employment of the particular enantiomer in the particular salt form would have been obvious since Reis teaches that all the enantiomer and pharmaceutical acceptable salts are similarly useful.

A person of ordinary skill in the art would have been motivated to employ the compounds herein for the treatment or prophylactic treatment of sepsis, including for those patients suffering from bacteraemia because antithrombotic agents are known to be useful for treatment of sepsis. The employment of the particular compound as the antithrombotic agent is obvious as it is disclosed as one of the preferred compounds. The employment of the particular enantiomer in the particular salt form would have been obvious since Reis teaches that all the enantiomer and pharmaceutical acceptable salts are similarly useful. Furthermore, one of the ordinary skill would have found it obvious to employ a stereoisomer of the known antithrombotic compounds herein in the claimed method since it is considered within the skill of the art to resolve the optical isomers of a known chiral compound, and each isomer is expected to be active in the absence of evidence to the contrary. See In re Anthony 162 USPQ 594; In re Adamson 125 USPQ 233.

Finally, the further employment of another antithrombotic agents, such as antithrombin, would have been obvious to one of ordinary skill in the art, because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art;

Art Unit: 1617

thus , the claimed invention which drawn to the employment of a combination of two known antithrombotic agents sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069.

Response to the Arguments

Applicants' amendments and remarks submitted April 3, 2007 have been fully considered. The amendments are persuasive as to the rejections under 35 U.S.C. 112 first paragraph, but are not persuasive for the rejections set forth above.

8. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, it would have been obvious to use antithrombotic agents for treatment of sepsis, as the references, as whole, show the usefulness of various antithrombotic agents for treatment of sepsis, regardless of the underline biochemical mechanism of those antithrombotic agents.

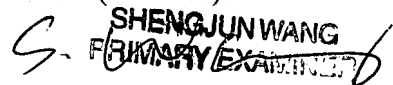
9. Applicants assert that Romisch et al. (EP 1 027 894), Tsukada et al. (EP 0 781 558) and Iqbal et al. teach away from the claimed invention because each of the references teaches antithrombotic agents with different biological mechanisms. The arguments are not persuasive. Particularly, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). The references as a whole have clearly suggested that antithrombotic agents are useful for treatment of sepsis regardless of the biochemical mechanism.

Art Unit: 1617

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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